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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/827,383	04/04/2001	Michael Mittmann	04537.005 / 3108.1	6376

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EXAMINER	
FREDMAN, JEFFREY NORMAN	
ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 01/31/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/827,383	MITTMANN ET AL.	
	Examiner	Art Unit	
	Jeffrey Fredman	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,7 and 15-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,7 and 15-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *12/21/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

12/16/04

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 16, 2004 has been entered.

Claim Rejections - 35 USC § 101

2. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3. Claims 1, 2, 7, 15-19 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility.

The current claims are drawn to a set of nucleic acids tags with at least 1000 sequences whose sequences comprise SEQ ID NO: 1-2050, with SEQ ID Nos: 1-10 being selected.

Credible Utility

Following the requirements of the Utility Guidelines (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for Utility.), the first inquiry is whether a credible utility is cited in the specification for use of the nucleic acids. One cited utility identified in the specification is to analyze genomic DNA (see page 10, for example). This utility is credible.

Upon identification of credible utilities, the next issue is whether there are any well established utilities for the nucleic acid. No well established utilities for these specific SEQ ID Nos: 1-10 are identified in either the specification or in the cited prior art.

Substantial utility

Given the absence of a well established utility, the next issue is whether substantial utilities are disclosed in the specification. Here, there is no evidence of any substantial utility. No substantial use for a set of sequences comprising SEQ ID NOs: 1-10 is found in the specification nor is there any use for the method or system involving SEQ ID NO: 1.

As noted in the utility guidelines, methods of treating unspecified diseases, basic research on a product to identify properties, intermediate products which themselves lack substantial utility are all insubstantial utilities (see page 6 of the Utility guideline training materials). If there were evidence of the association of SEQ ID NO: 1 with any disease state, with a protein activity or with some other biological phenotype, this evidence might be considered regarding a substantial utility. However, no such evidence is found. At best, the utilities of analyzing genomic DNA are indicative that SEQ ID NOs: 1-10 are intermediate products which lack substantial utility.

In the Supreme Court case of *Brenner v. Manson*, 148 U.S.P.Q. 689 (1966), a novel compound which was structurally analogous to other compounds that were known to possess anti-tumor activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that

all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately apparent or fully disclosed "real world" utility. The court held that:

> The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. . . . [u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field. . . . a patent is not a hunting license. . . .[i]t is not a reward for the search, but compensation for its successful conclusion.

The instant claims are drawn to a set of polynucleotides with no known function. The specification does not teach the function of any of the nucleic acids to which these sequences hybridize. The function of these nucleic acids is as yet undetermined with no known biological significance. There is no evidence of record or any line of reasoning that would support a conclusion that the nucleic acid of the instant application was, as of the filing date, useful for any specific assay or therapeutic use. Until some actual and specific significance can be attributed to the nucleic acid, one of ordinary skill in the art would be required to perform additional experimentation in order to determine how to use the claimed invention. Following both the Utility Guidelines and the direction of the Supreme Court of the United States in Brenner, there is no specific benefit in using a set of these specific sequences. Thus, there is no immediately substantial or "real world" utility as of the filing date.

Specific Utility

In the current case, even if the substantial utility argument above were found unpersuasive, there is clearly no specific utility. To the extent that the nucleic acid and polymorphisms in SEQ ID NO: 1-10 can be used in genomic analysis assays, this utility is not at all specific to SEQ ID NO: 1-10. Literally any sequence would function in a genome analysis assay as described in the specification. As the utility guideline training materials note on page 5-6 regarding specific utility that "a claim to a polynucleotide whose use is disclosed simply as a 'gene probe' or 'chromosome marker' would not be considered to be *specific* in the absence of a disclosure of a specific DNA target (italics in original)". Here, there is no disclosure of any specific use of SEQ ID NO: 1-10 that is not shared with any other sequence.

Further, the sequences are not even species or chromosome specific, based upon the sequence search. As the attached search of SEQ ID NO: 3 in Genbank demonstrates, result 3 shows an 90% match (local similarity) to a sequence in chromosome 14 of humans while result 13 shows an 89.5% match (local similarity) to human chromosome 8. Further, the remaining results show similarity to Pseudomonas, Lotus, Rats and Rice with equivalent levels of local similarity. Similar results exist for the other 9 probes. So the sequences claimed lack 100% specificity to any particular organism in Genbank, and the specification lacks any discussion of the target for these oligonucleotides. Consequently, there is no specific target for any of the claimed sequences. With regard to the utility analysis, the current situation directly tracks Example 9 of the utility guidelines, where an unknown nucleic acid fragment of entirely unknown function was characterized as lacking utility.

Finally, there appears to be no element which is unique to the selected sequences. That is, the ability of the array to be used in SNP-IT™ assays, for example, is not sequence dependent. That is, there is nothing specific to the 2050 sequences of the current claim which distinguish these sequences from a different set of 2050 sequences or from any set of 2050 unrelated sequences.

Therefore, a set of nucleic acids comprising SEQ ID NO: 1-10 has no specific utility.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1, 2, 7, 15-19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Nature of Invention

The current claims drawn to a set of nucleic acids tags with at least 1000 sequences whose sequences comprise SEQ ID NO: 1-2050, with SEQ ID Nos: 1-10 being selected. The nature of this invention is in nucleic acid analysis of a particular sequence with no other associated information. The invention is in an class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and

biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001).

Breadth of the claims

The claims are drawn to a set of nucleic acids comprising at least 1000 sequences from SEQ ID Nos: 1-2050, and for which SEQ ID Nos: 1-10 were selected.

Amount of Guidance in the Specification

The specification discloses the entire sequence of SEQ ID NOs: 1-10, but identifies no particular use for the sequence. In particular, the specification lacks any discussion of the target of SEQ ID NOS: 1-10, or of any of the 2040 other sequences. As noted in the utility rejection above, this utility is not found to be substantial nor specific and consequently, the specification provides NO guidance regarding how to use SEQ ID NO: 1. The general guidance that the method is useful in methods of genomic analysis fails to provide the specific details necessary to apply sequences whose targets are unknown to such genomic analysis.

Working Examples

There are working examples in which the sequences are hybridized. However, there are no working examples in which SEQ ID NOs: 1-10, or indeed any of the 2040 other sequences, are used in any assay for detection or diagnosis of any disease or any other related utility. No real world use or particular use is given for these sequences.

Amount of Guidance in Prior Art

As noted in the utility rejection above, the prior art provides no guidance with regard to the particular function of SEQ ID NOs: 1-10.

Skill in the Art

While no evidence is adduced, the examiner believes the skill in the art would be considered high.

Predictability of the Art

The art in biotechnology, as relates to the association of diseases with particular genes, is highly unpredictable. The claimed sequences currently appear to represent orphan genes, since no matches were identified in a sequence search. Regarding such Orphan genes, Dujon (Trends in Genetics (1996) 12(7):263-270) notes that the most striking result of yeast sequencing is that "a significant proportion of yeast genes are orphans of unpredictable function (abstract)". Dujon further states "We have no clue to which direction to search and, even worse, when considering the experiments that could be done on orphans, we rapidly find ourselves intellectually embedded in the schemes of the past (page 2169, column 2)." Thus, it is extremely unpredictable what to do with an orphan gene such as SEQ ID NOs: 1-10 in the absence of any defined utility.

Further, as noted above, the sequences are not even species or chromosome specific, based upon the sequence search. As the attached search of SEQ ID NO: 3 in Genbank demonstrates, result 3 shows an 90% match (local similarity) to a sequence in chromosome 14 of humans while result 13 shows an 89.5% match (local similarity) to human chromosome 8. Further, the remaining results show similarity to Pseudomonas, Lotus, Rats and Rice with equivalent levels of local similarity. Similar results exist for the other 9 probes. So the sequences claimed lack 100% specificity to any particular organism in Genbank, and the specification lacks any discussion of the target for these

oligonucleotides. Consequently, there is no specific target for any of the claimed sequences. In the absence of any target, it is entirely unpredictable how these sequences would function even in some sort of genomic analysis method. SEQ ID NO: 3, for example, would crosshybridize to both chromosomes 8 and 14 and would not give significant information regarding the presence or absence of any particular human, animal or plant sequence in a sample, since the sequence would hybridize about equally well to human, rat, rice and lotus, among other species.

Quantity of Experimentation

An immense amount of experimentation would be required in order to define whether any of these nucleic acids are associated with any particular disease state or other specific and substantial use. For example, in order to acquire statistically significant evidence of an association with a disease or other utility, one of the possible targets such as human patients, experimental rats, or rice and lotus plants in each of the many hundreds of different possible disease states would need to be subjected to collection of samples for analysis of their DNA, followed by analysis and the inventive efforts of determining if any association exists. This is a very large quantity of experimentation.

Determination

In view of the unpredictable nature of the invention, the absence of any guidance in the specification for a substantial and specific use, the absence of any working examples in the specification, the negative teachings in the prior art, the extreme unpredictability of the invention, and the large amount of experimentation necessary balanced against the high level of skill in the art and the relatively narrow breadth of the

claims, it is concluded that undue experimentation would be required to use this invention as claimed.

Response to Arguments

6. Applicant's arguments filed March 4, 2004 have been fully considered but they are not persuasive.

Applicant argues that the tag probes may be used in methods such as single base extension. This argument is not persuasive for several reasons. The single base extension method involves a specific interaction of a primer adjacent to a known mutagenic site and a single, usually dideoxynucleotide terminator, is added to the primer. This method relies upon specific placement of the primers immediately adjacent to known mutation sites. Applicant's sequences are not adjacent to such sites and Applicant has not presented any evidence that any of the primers would function to detect allelic variants at any particular site. As shown in the rejection above, the single members selected from the claimed sequences have equal homology to different chromosomes in human as well as many other nonhuman and even nonmammalian species. So there is no expectation that the method would function in a single base extension type assay.

If the utility is solely that these sequences can be used as tags, there is nothing specific about this utility. ANY sequence can be used as tags. Applicant's argument that the mere selection of the sequences to have similar lengths and melting temperatures provides a specific utility to the set of sequences is not found persuasive because it fails to provide anything that distinguishes this set from any other set of

capture probes. All sets of capture probes are designed to have matched Tm's and to bind specifically to their cognate target. This random selection of random sequences does not provide any specific utility for the claimed invention.

Applicant then argues that there is utility because a paper cites the use of a different array, with 32,000 probes, as evidence that the current array would be useful in the same method. The issue is not whether the invention can be used, but whether there is a specific utility under the utility guidelines and the caselaw.

Applicant concludes the utility arguments by noting that there would be an almost infinite number of probes which would not meet the criteria set by Applicant for the particular set selected. While this is true, it is equally true that there would be an almost infinite number of sets of probes, distinct from those taught by Applicant, which would meet the criteria selected by Applicant. So there is nothing particularly specific about the set chosen by Applicant. In the paper cited by Applicant, there are at least 30,000 more probes than those shown in this specification. Given that the number of possible probes is 4^{20}, or 1,099,511,627,776 different possibilities, the number of possible probe sets is immense. There is no specific utility for Applicant's probe set since the set has no unique features whatsoever.

Applicant then argues the enablement rejection. Since the enablement rejection is based upon the utility rejection and the failure of a patentable use for the invention, and since the utility rejection is maintained, the enablement rejection is also maintained.

Conclusion

7. All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jeffrey Fredman
Primary Examiner
Art Unit 1637
1/25/05